26 and 30, as well as page 2, line 25 to page 3, line 11; page 5, lines 23-28; and page 6, line 19 to page 9, line 33.

No new matter is believed to have been added by these amendments.

REMARKS

Claims 1-9, 15, 20-24, and 26-40 are pending in the present application.

Applicants respectfully request entry and reconsideration in view of the following comments which were filed, but not entered, on April 3, 2003. In addition, Applicants would like to thank Examiner Haddad for the helpful and courteous telephone discussion with their undersigned Representative on February 3, 2003.

The present invention relates to "a composition to induce mucosal immunization," as claimed in Claims 26 and 30. More specifically, the present invention relates to a lipopeptidic composition that induces a stronger systemic immune response in a mammal when administered mucosally.

In a particular embodiment, the invention concerns the administration to a mammal of a lipopeptidic composition wherein the peptidic region is derived from *Plasmodium falciparum* antigens, as those disclosed in the specification, conferring protection against paludism (malaria; see Claims 37 and 40).

The rejections of Claims 26-33 under 35 U.S.C. §102 over Perlaza et al is traversed.

The novelty of the present invention resides in the fact that a peptide having a lipid tail is imparted with an ability to cross the mucous membrane (see page 3, lines 18-20 and the Examples). When the lipid-tailed peptides reach the dendritic cells, which are antigen presenting cells presented in the subcutaneous tissue or submucosal tissue, antigenic information is transmitted to the lymphocytes. Under the effect of said information,

lymphocytes are able to react by starting a specific immunological reaction. In contrast to the inventive formulation of the lipopeptidic composition, peptides alone cannot cross the mucous membrane. This advantage has been clearly set forth in the specification at page 3, lines 18-26, which states:

> "... the present invention provides a method of inducing an immune response, by the delivering of an effective amount of a lipid-tailed polypeptide, also referred to as lipopolypeptide herein or lipoprotein, to a mucosal membrane of a subject.
>
> Using antigen-specific T-helper cell responses and the production of serum antibodies to probe the immune response, we now show that intranasal or sub-lingual immunization with lipid-tailed of polypeptides could represent an interesting alternative route: strong systemic immune responses were observed, which were compared to the immune responses obtained in parallel experiments in which the same immunogen was delivered by subcutaneous route."

Moreover, the figures and the descriptions thereof underscore the advantages of the composition *consisting essentially of* the claimed lipid-tailed peptides, administered by mucosal route and inducing strong systemic immune response, over composition consisting of peptides alone.

Which is really important is not the capability of the composition of the invention to induce a protection, but the fact that it is able to induce a strong immune systemic response by simply depositing it on the oral, or nasal membrane. Accordingly, by the present invention, the commonly employed delivery method of using a syringe and needle may be replaced.

With specific reference to Perlaza et al, Applicants note that:

- Perlaza et al do not disclose a composition *consisting essentially of* lipid-tailed peptides to induce a strong systemic immune response when administered by mucosal route as does the composition claimed in the pending application (see Applicants arguments presented in the Amendment and Request for Reconsideration filed on September 30, 2002).

- Applicants disagree with the Examiner's assertion that: "Products of identical chemical composition cannot have mutually exclusive properties" (paper number 16, page 7, line 1).

As a proof of the distinction between the properties of the composition of Perlaza et al and the present invention, Applicants wish to draw the Examiner's attention to Figures 1 and 3, which illustrates the results obtained in the present application and which establishes a comparison between various administration routes of the same chemical composition. Clearly, same lipid-tailed peptides (identical chemical composition) have not always the same properties (quantitative and qualitative differences in inducing systemic immure response) and it is these properties, which are present in Claims 26 and 30 which clearly distinguish the claimed invention from that of Perlaza et al.

Effectively, neither the quantitative response (amount of detected specific antibodies raised against the peptide), nor qualitative response (specific antibodies of IgG2A isotype are raised when mucosal administration is used, versus specific antibodies of ISM isotype when the same composition is administered by subcutaneous route) are the same.

These different properties are also duly identified in the present specification at page 3, lines 26-31:

> "Qualitative differences were observed when comparing parenteral or transmucosal immunization routes, with a dominant IgGI observed after parenteral immunization versus a preferential IgG2 a isotype response far the mucosal route, suggesting that distinct antigen presenting cells were involved. Mucosal immunization by lipidated polypeptides appears therefore as a novel, cost-effective and noninvasive approach that does not require the use of extraneous adjuvant."

Therefore, it is clear that Perlaza et al, which may disclose lipid-tailed peptides, do not disclose any composition to induce systemic immune response when administered mucosally. In fact, the only reference to an administration route by Perlaza et al is found in

page l, column 2, which only refers to subcutaneous immunizations, as well as a footnote in Table 1 that specifies that lipopetides were "*injected.*"

Applicants note that the standard for determining anticipation requires that the reference "must teach every element of the claim" (MPEP §2131). Therefore, in view of the absence of a disclosure or suggestion of any composition to induce systemic immune response when administered mucosally as presently claimed, Perlaza et al do not anticipate the presently claimed invention.

Withdrawal of this ground of rejection is requested.

The rejections of Claims 26-33 under 35 U.S.C. §112, first paragraph (written description and enablement), is obviated in part by amendment and traversed in part.

At the outset, Applicants have replaced the objected to term "having" with the more conventional term "comprising." In addition, Applicants note that a keyword search of the "Patent Full-Text and Full-Page Image Databases" on the U.S.P.T.O. web-site for the years 1976 to present reveals 177 patents that have issued with the phrase "comprising the sequence of SEQ ID NO:". On April 3, 2003, Applicants submitted U.S. Patent Number 6,495,743 evidencing the fact that the U.S. Patent Office has taken the position that the phrase "comprising the sequence of SEQ ID NO:" is appropriate and acceptable.

Moreover, Applicants do not agree with the Examiner's assertion that the Applicant is not in possession of any other composition than those consisting of tailed-lipid peptides referring to sequences SEQ ID NO:1, SEQ ID NO:2 and SEQ ID NO:3, nor when he asserts that conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred.

On April 3, 2003, Applicants also submitted BenMohamed L. et al (Eur. J. Immunol. 2002, **32**: 2274-2281) in which the inventors/authors disclose that they were able to induce a

systemic immune response with other antigens and in accordance with the present specification in that "lipopeptides derived from herpes and cytomegalovirus showing that this mode of mucosal immunization extends to other antigens" (page 5, paragraph 2.4, last sentence, and figure 3C). If the Examiner is unable to locate this previously submitted BenMohamed L. et al, he is invited to contact Applicants' undersigned Representative who would be happy to resubmit this reference.

Based on the foregoing, Applicants submit that the present claims fully comply with the requirements of 35 U.S.C. §112, first paragraph (written description and enablement). Withdrawal of these grounds of rejection are requested.

The rejection of Claims 26-33 under 35 U.S.C. §112, first paragraph, as containing "new matter" is traversed.

First, the Examiner has rejected the claims based on the addition of the "limitation" of "consisting essentially of." Applicants remind the Examiner that the phrase "consisting essentially of" is *not* actually a limitation, but rather is a transitional phrase. To refresh the Examiner's memory, Applicants reproduce the relevant section of MPEP §2111.03, which states: "The transitional phrases "comprising," "consisting essentially of" and "consisting of" define the scope of a claim with respect to what unrecited additional components or steps, if any, are excluded from the scope of the claim."

Therefore, the transitional phrase recited in the claims is a *matter of choice* and serves to announce to the artisan the scope of the claim and what unrecited additional components or steps are excluded from the claim. The absence of a specific recitation of the transitional phrase in the specification is of no moment and the Applicant is free to choose which transitional phrase best defines his/her invention. Accordingly, Applicants submit that the recitation of "consisting essentially of" in the claims does not constitute "new matter."

With respect to the term "malaria infection," the Examiner appears to be concerned that Applicants did not point specifically to where in the specification support for this term may be found, even though the Examiner clearly recognizes the presence of such support at page 3, line 1 (see paper number 18, page 2, lines 29-30). In order to clearly demonstrate to the Examiner that the term "malaria infection" finds full support in the specification, Applicants point to page 2, line 25 to page 3, line 11; Figure 2 and the description at page 4 lines 20-24, page 5, lines 23-28; and page 6, line 19 to page 9, line 33. In addition, when referring to these sections, Applicants remind the Examiner that *Plasmodium falciparum* is an organism responsible for malaria. This fact is clearly supported by the art of record, as well as the present specification at page 2, line 25 to page 3, line 11. Therefore, Applicants submit that the recitation of "malaria infection" in the claims does not constitute "new matter."

Withdrawal of this ground of rejection is requested.

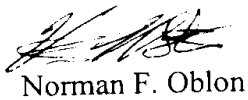
Finally, on April 3, 2003, Applicants submitted an Information Disclosure Statement (Form PTO-1449) with a Statement of Relevancy and an English Translation of EP 0 491 628. For the Examiner's convenience and to ensure entry and consideration thereof, Applicants submit herewith a copy of Form PTO-1449 and the Statement of Relevancy originally submitted on April 3, 2003 along with a copy of the date-stamped filing receipt evidencing timely filing thereof. An indication that the English Translation of EP 0 491 628 has been considered is requested at the Examiner's next opportunity. If the Examiner is unable to obtain the English Translation of EP 0 491 628 from the April 3, 2003 submission, it is requested that the Examiner contact Applicants' undersigned Representative at his earliest convenience so as to avoid any further delay in examination.

Applicants submit that the present application is now in condition for allowance.

Early notification of such action is earnestly solicited.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.



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IN THE CLAIMS

Please amend the claims as follows:

26. (New) A composition consisting essentially of a lipopeptide [having a] comprising the sequence of LSA3-NRII Ac-LEESQVNDDIFNSLVKSVQQEQQHNVK(PAM)NH2 (SEQ ID NO:2), [without adjuvant, capable of inducing a mucosal protection in vivo against a malaria infection] capable of inducing an immune systemic response specific to said sequence when administered via a mucosal route without adjuvant.

30. (New) A composition consisting essentially of a lipopeptide [having a] comprising the sequence of LSA1-J Ac-ERRAKEKLQEQQSDLEQRKADTKKK(PAM) (SEQ ID NO:3), [without adjuvant, capable of inducing a mucosal protection in vivo against a malaria infection] capable of inducing an immune systemic response specific to said sequence when administered via a mucosal route without adjuvant.